Aflibercept 8 mg in Treatment-Naive Macular Edema Secondary to Retinal Vein Occlusion: Primary Endpoint Results from the QUASAR Study

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Disclosures

- Jordana G. Fein has served as a consultant for Regeneron Pharmaceuticals, Inc., Bausch and Lomb, Genentech/Roche, and Apellis; and has served on a speaker's bureau for Regeneron Pharmaceuticals, Inc., Genentech/Roche, and Apellis Pharmaceuticals
- The QUASAR trial (ClincalTrials.gov: NCT05850520) is sponsored by Bayer AG (Leverkusen, Germany). The sponsor participated in the design and conduct of the study, analysis of the data, and preparation of this abstract
- This study includes research conducted on human patients. Institutional review board/institutional ethics committee approval was obtained prior to study initiation
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- The QUASAR study investigators wish to thank all patients and investigators of the QUASAR trial

QUASAR Study Design

Multicenter, randomized, double-masked study in patients with treatment-naive macular edema secondary to RVO
Randomized at baseline 1 (2q4) : 1 (8q8/3) : 1 (8q8/5)

2q4
Aflibercept 2 mg every 4 weeks
n=301

8q8/3
Aflibercept 8 mg every 8 weeks after 3 initial monthly injections
n=293

8q8/5
Aflibercept 8 mg every 8 weeks after 5 initial monthly injections
n=298

Primary endpoint at Week 36
Change from baseline in BCVA (non-inferiority)

Secondary endpoints at Week 36
Number of active injections from baseline
Change from baseline in CRT

End of study at Week 64

BCVA, best-corrected visual acuity; CRT, central retinal thickness; DRM, dose regimen modification; RVO, retinal vein occlusion; 2q4, aflibercept 2 mg administered every 4 weeks; 8q8/3, aflibercept 8 mg administered every 8 weeks, after 3 initial monthly injections; 8q8/5, aflibercept 8 mg administered every 8 weeks, after 5 initial monthly injections.

QUASAR Dosing Regimen

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36
2q4	X	X	X	X	X	X	X	X	X[b]	T&E
8q8/3	X	X	X	o	X[a]	o	X[a]	O	X[a,b]	T&E
8q8/5	X	X	X	X	X	o	X[a]	O	X[a]	o

☐ indicates reference visit for DRM assessment (Week 12 for 8q8/3 and Week 20 for 2q4 and 8q8/5)

Primary endpoint
Mean change in BCVA (noninferiority)

[a]DRM: Interval Shortening

- Patients in the 8q8/3, 8q8/5, and 2q4 groups could qualify for interval shortening at a dosing visit beginning at Week 16, 24, and 40, respectively
- ***Criteria for interval shortening:***
  - >5-letter loss in BCVA from reference visit[c]
    AND
  - >50-µm increase in CRT from reference visit[c]
- Dosing intervals were shortened by 4-week increments if patients met the DRM criteria and their last dosing interval was ≥Q8

[b]DRM: Interval Extension

- Patients in the 2q4 and 8q8/3 groups could qualify for interval extension at a dosing visit beginning at Week 32 and those in 8q8/5 qualified at Week 40
- ***Criteria for interval extension:***
  - <5-letter loss in BCVA from reference visit[c]
    AND
  - CRT <320 µm on Heidelberg Spectralis (<300 µm on Cirrus or Topcon SD-OCT)
- Dosing intervals were extended by 4-week increments if DRM criteria were met

[c]Reference visit defined as Week 12 for 8q8/3 and Week 20 for 8q8/5 and 2q4.
Stippled boxes = initial treatment phase; X = active injection; o = sham injections. Figure does not reflect all dosing options if the intervals are shortened.
Q4, every 4 weeks; SD-OCT, spectral domain-optical coherence tomography; T&E, treat and extend; Wk, week.

Key Eligibility Criteria

Inclusion Criteria

- Adults (≥18 years) with treatment naive macular edema secondary to RVO (BRVO, CRVO, or HRVO) diagnosed within 16 weeks of screening visit
- BCVA of 73 to 24 ETDRS letters (Snellen equivalent 20/40 to 20/320)
- Decrease in BCVA determined to be primarily the result of RVO
- Mean CRT ≥320 µm on Heidelberg Spectralis or ≥300 µm on Cirrus or Topcon SD-OCT, as confirmed by the reading center

Exclusion Criteria

- Concurrent disease that causes substantial decrease in BCVA, is expected to limit BCVA recovery or is likely to require medical or surgical intervention during the study in the study eye
- Advanced nAMD or geographic atrophy, diabetic macular edema, and diabetic retinopathy
- Uncontrolled glaucoma (IOP >25 mmHg despite anti-glaucoma medication) in the study eye

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ETDRS, Early Treatment Diabetic Retinopathy Study; HRVO, hemiretinal vein occlusion; IOP, intraocular pressure; nAMD, neovascular age-related macular degeneration.

QUASAR Study Sites

QUASAR is a **global** study conducted at 237 sites in 27 countries

Patient Disposition at Week 36

	2q4	8q8/3	8q8/5	Total
Randomized, n	302	294	298	894
Treated, n (%)	301 (99.7)	293 (99.7)	298 (100)	892 (99.8)
Completing Week 36, n (%)	287 (95.0)	278 (94.6)	273 (91.6)	838 (93.7)
Discontinued before Week 36, n (%)	14 (4.6)	15 (5.1)	25 (8.4)	54 (6.0)
Reasons for discontinuation, n (%)				
Withdrawal by patient	8 (2.6)	8 (2.7)	16 (5.4)	32 (3.6)
Adverse events	2 (0.7)	0	2 (0.7)	4 (0.4)
Death	2 (0.7)	2 (0.7)	3 (1.0)	7 (0.8)
Lost to follow-up	2 (0.7)	3 (1.0)	3 (1.0)	8 (0.9)
Other[a]	0	2 (0.7)	1 (0.3)	3 (0.3)

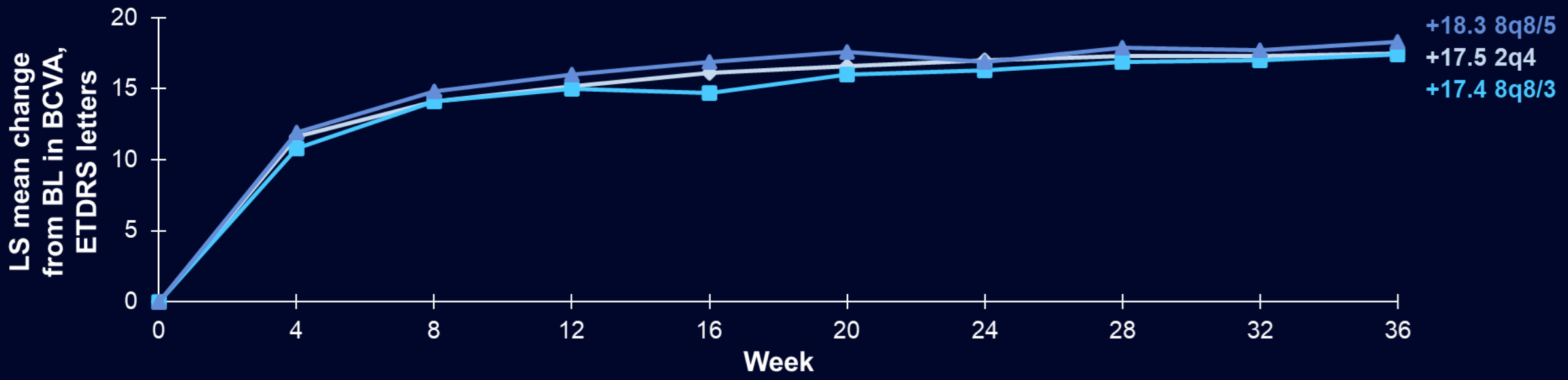
[a]Includes "logistical problem," "physician decision," and "protocol deviation." Categories were combined to maintain masking of individual patients.

Baseline Demographics and Disease Characteristics

	2q4 (n=301)	8q8/3 (n=293)	8q8/5 (n=298)	Total (n=892)
Age, years	65.9 (11.7)	65.8 (11.5)	65.8 (11.5)	65.9 (11.6)
Female, n (%)	144 (47.8)	136 (46.4)	146 (49.0)	426 (47.8)
Race, n (%)				
Asian	101 (33.6)	91 (31.1)	97 (32.6)	289 (32.4)
Black or African American	8 (2.7)	7 (2.4)	9 (3.0)	24 (2.7)
White	178 (59.1)	173 (59.0)	177 (59.4)	528 (59.2)
Other[a]	1 (0.3)	0	4 (1.3)	5 (0.6)
Not reported	13 (4.3)	22 (7.5)	11 (3.7)	46 (5.2)
Hispanic or Latino, n (%)	22 (7.3)	25 (8.5)	14 (4.7)	61 (6.8)
History of hypertension, n (%)	187 (62.1)	192 (65.5)	196 (65.8)	575 (64.5)
RVO type, n (%)[b]				
BRVO	149 (49.5)	159 (54.3)	159 (53.4)	467 (52.4)
CRVO	117 (38.9)	99 (33.8)	102 (34.2)	318 (35.7)
HRVO	35 (11.6)	35 (11.9)	37 (12.4)	107 (12.0)
BCVA, ETDRS letters	54.1 (14.3)	55.2 (13.6)	55.4 (13.4)	54.9 (13.8)
CRT, µm[c]	651 (240)	626 (230)	609 (213)	629 (229)

FAS. Data are mean (SD) unless otherwise indicated.
[a]Includes American Indian or Alaskan native, native Hawaiian or other Pacific Islander, and Multiple. [b]Assessed by the reading center. [c]Baseline CRT measurement was missing for 1 patient in the 2q4 group. FAS, full analysis set; SD, standard deviation.

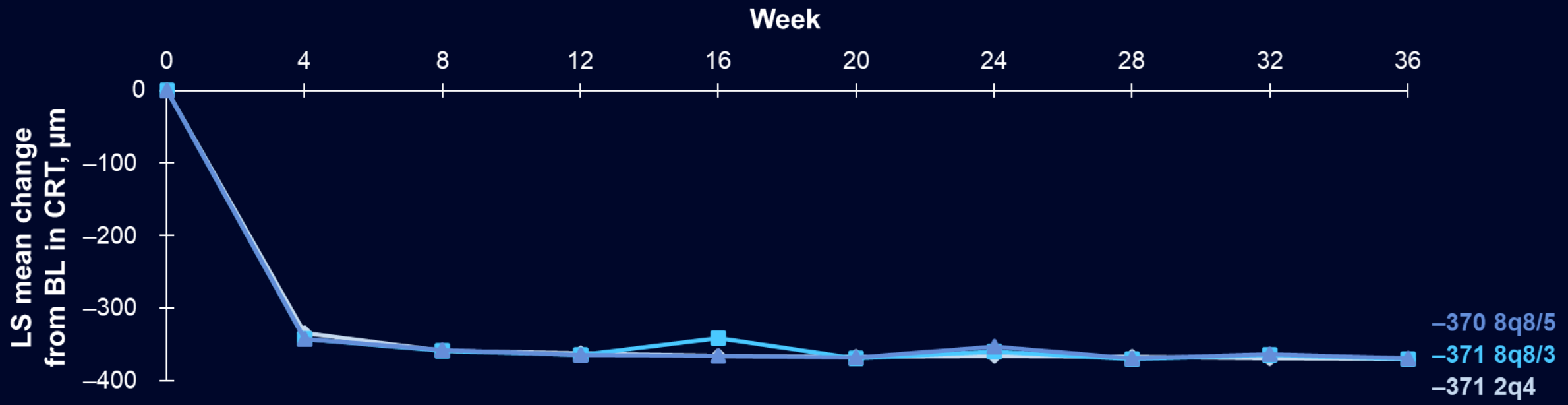
Both Aflibercept 8 mg Groups Achieved Non-inferior BCVA Gains Compared to 2q4 at Week 36 with Fewer Injections



	Absolute mean BCVA at Week 36[a]	LS mean change from BL at Week 36	Difference in LS means versus 2q4	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin	Mean number of injections through Week 36[a]
2q4 (n=301)	72.0	17.5				8.5
8q8/3 (n=293)	72.8	17.4	–0.1	–2.0, 1.9	*P*<0.0001	6.0
8q8/5 (n=298)	74.6	18.3	0.8	–1.1, 2.7	*P*<0.0001	6.7

FAS. LS means were generated using a mixed model for repeated measures with baseline BCVA as a covariate; treatment group (aflibercept 8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asian-Pacific vs Europe vs America], BL BCVA [<60 vs ≥60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between baseline BCVA and visit and treatment and visit. [a]Observed values (censoring data post-ICE). BL, baseline; CI, confidence interval; ICE, intercurrent event; LS, least squares; 2q4, aflibercept 2 mg administered every 4 weeks; 8q8/3, aflibercept 8 mg administered every 8 weeks, after 3 initial monthly injections; 8q8/5, aflibercept 8 mg administered every 8 weeks, after 5 initial monthly injections, [a]Safety analysis set

Both Aflibercept 8 mg Groups Achieved Robust CRT Reductions Compared to 2q4 at Week 36 with Fewer Injections

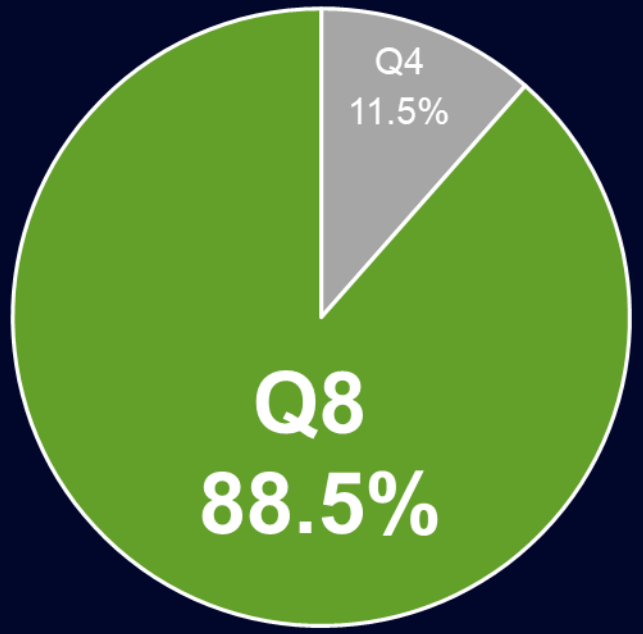


	Absolute mean CRT (µm) at BL	Absolute mean CRT (µm) at Week 36[a]	LS mean change from BL at Week 36	Mean number of injections through Week 36[a]
2q4 (n=301)	651	257	–371	8.5
8q8/3 (n=293)	626	258	–371	6.0
8q8/5 (n=298)	609	259	–370	6.7

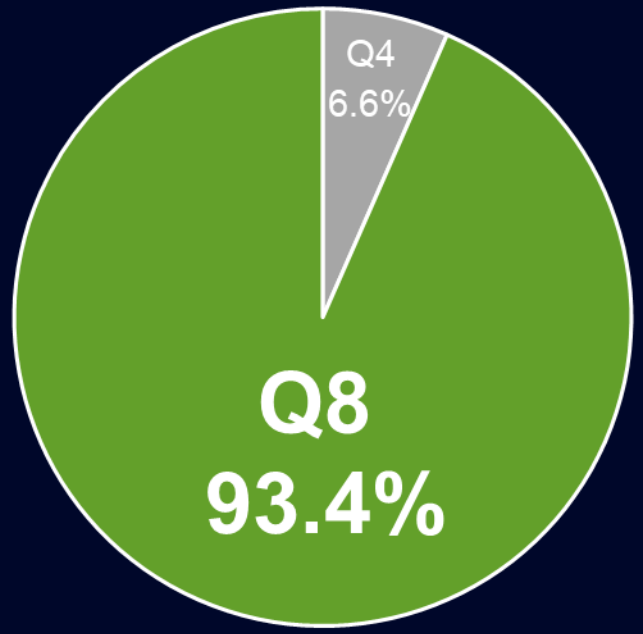
FAS. LS means were generated using a mixed model for repeated measures with baseline CRT as a covariate; treatment group (aflibercept 8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asian-Pacific vs Europe vs America], BL BCVA [<60 vs ≥60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between baseline CRT and visit and treatment and visit. [a]Observed values (censoring data post-ICE).

2q4, aflibercept 2 mg administered every 4 weeks; 8q8/3, aflibercept 8 mg administered every 8 weeks, after 3 initial monthly injections; 8q8/5, aflibercept 8 mg administered every 8 weeks, after 5 initial monthly injections, [a]Safety analysis set

Majority of Aflibercept 8 mg Patients Maintained Q8 Dosing Through Week 36



8q8/3
(n=278)

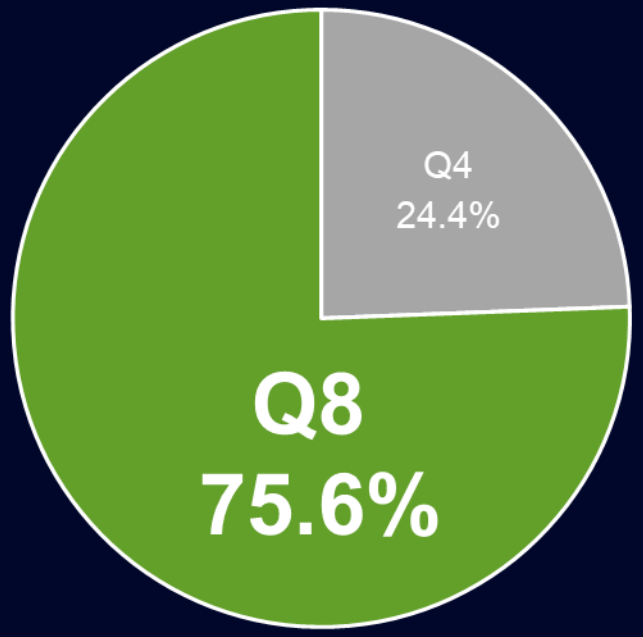


8q8/5
(n=273)

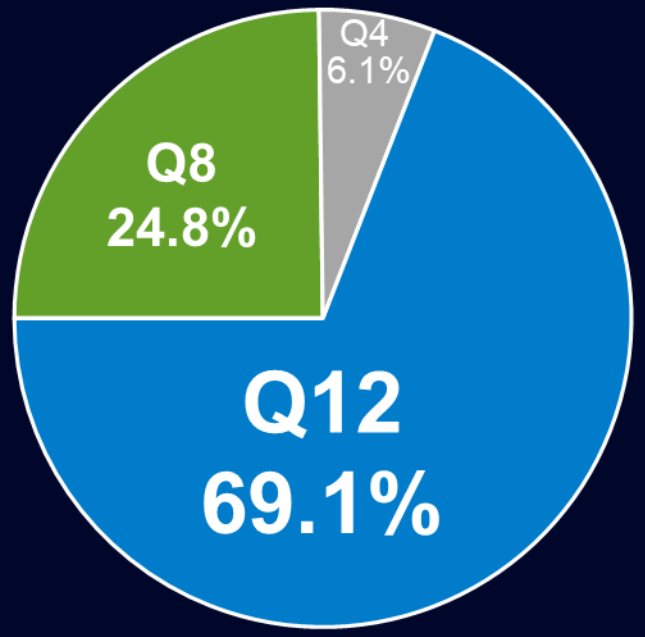
88.5% in the 8q8/3 group and 93.4% in the 8q8/5 group maintained Q8 dosing as per the treatment arm regimen without the need for interval shortening

Safety analysis set, patients who completed Week 36. Patients in the aflibercept 8 mg groups with a >5-letter loss in vision and a >50-µm increase in CRT compared to reference visit (Week 12 for 8q8/3 and Week 20 for 8q8/5) had their dosing interval shortened to Q4.
Q4, every 4 weeks; Q8, every 8 weeks.

Last Assigned Dosing Interval at Week 36 for Patients Eligible for Interval Extension



2q4
(n=287)

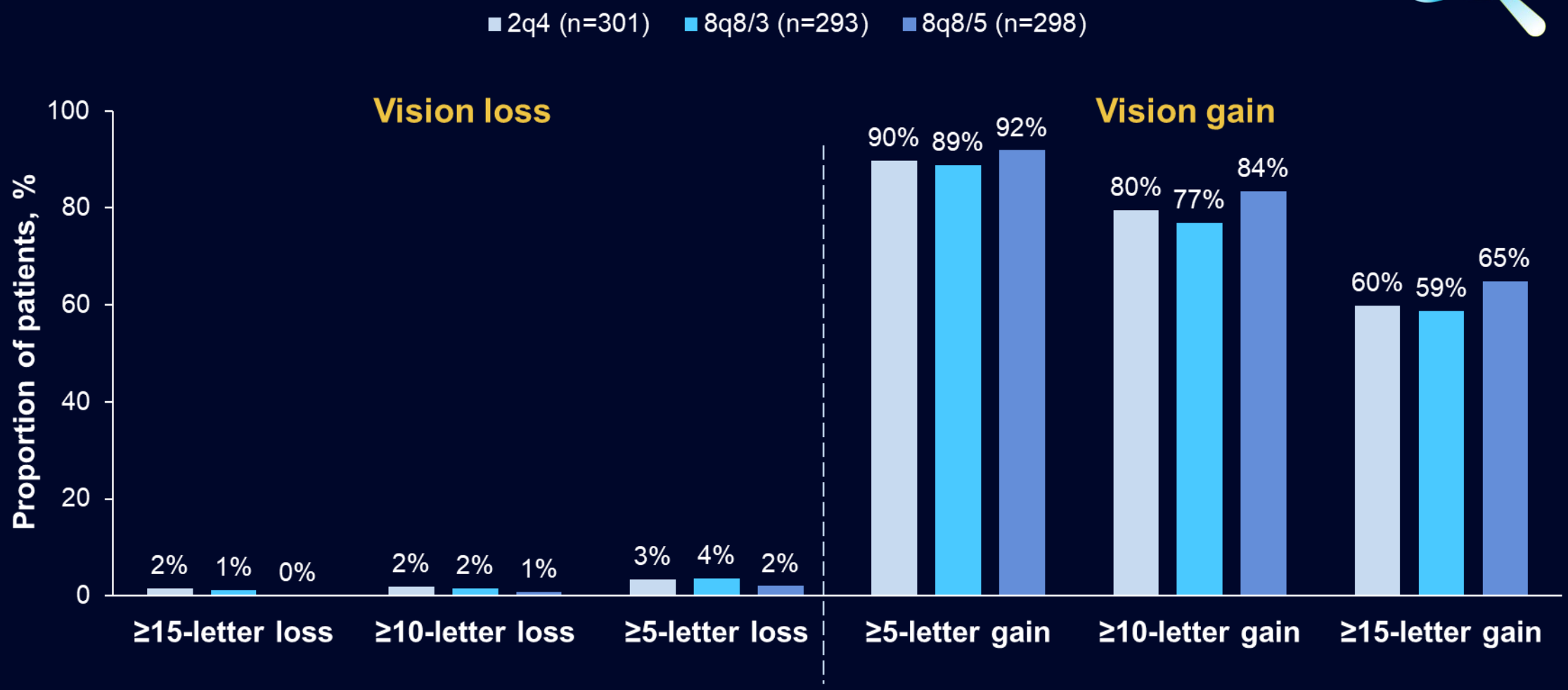


8q8/3
(n=278)

Per study design, dosing interval extension was not possible in the 8q8/5 group until Week 40

Safety analysis set, patients who completed Week 36.
Q12, every 12 weeks.

Proportion of Patients With ≥5-, 10- or 15-Letter Loss or Gain at Week 36



FAS, observed values (censoring data post-ICE).

Ocular and Non-Ocular Safety Through Week 36

	2q4 (n=301)	8q8/3 (n=293)	8q8/5 (n=298)	All 8 mg (n=591)
Ocular TEAEs, n (%)	98 (32.6%)	117 (39.9%)	97 (32.6%)	214 (36.2%)
Ocular SAEs, n (%)	8 (2.7%)	4 (1.4%)	4 (1.3%)	8 (1.4%)
Intraocular inflammation, n (%)	4 (1.3%)	2 (0.7%)	1 (0.3%)	3 (0.5%)
Anterior chamber cell	1 (0.3%)	0	0	0
Eye inflammation	1 (0.3%)	0	0	0
Iritis	0	1 (0.3%)	0	1 (0.2%)
Uveitis	0	0	1 (0.3%)	1 (0.2%)
Endophthalmitis	2 (0.7%)	1 (0.3%)	0	1 (0.2%)
Non-ocular SAEs, n (%)	26 (8.6%)	22 (7.5%)	28 (9.4%)	50 (8.5%)
APTC events, n (%)	5 (1.7%)	0	3 (1.0%)	3 (0.5%)
Deaths, n (%)	2 (0.7%)	2 (0.7%)	3 (1.0%)	5 (0.8%)

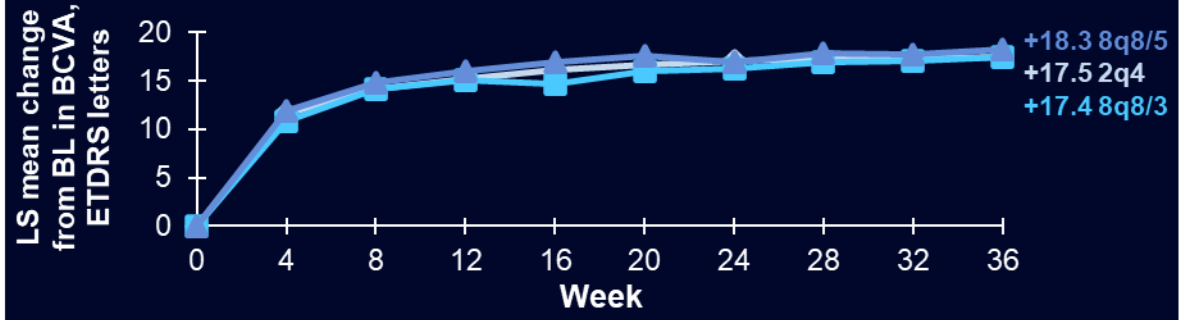
- No cases of occlusive retinal vasculitis were reported
- The safety profile of aflibercept 8 mg was consistent with the established safety of aflibercept 2 mg

Safety analysis set. Ocular TEAE and SAE data are presented for the study eye.
APTC, Anti-Platelet Trialists' Collaboration; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Conclusions

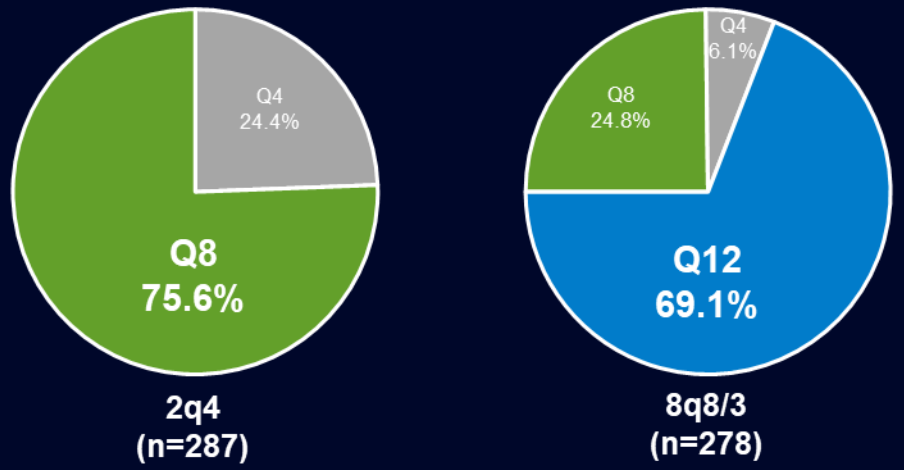
- Aflibercept 8q8/3 and 8q8/5 achieved **non-inferior BCVA gains and robust reductions in CRT with fewer injections** compared with 2q4 at Week 36
- The vast majority of patients in the aflibercept 8-mg groups **maintained ≥ Q8 dosing** through Week 36 without interval shortening
- The safety profile of aflibercept 8 mg in patients with macular edema secondary to RVO was **consistent with the established safety of aflibercept 2 mg and 8 mg**

Mean Change in BCVA Through Week 36[a]



	Absolute mean BCVA at Week 36[b]	LS mean change from BL at Week 36	Difference in LS means versus 2q4	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin	Mean number of injections through Week 36[c]
2q4 (n=301)	72.0	17.5				**8.5**
8q8/3 (n=293)	72.8	17.4	–0.1	–2.0, 1.9	*P*<0.0001	6.0
8q8/5 (n=298)	74.6	18.3	0.8	–1.1, 2.7	*P*<0.0001	6.7

Last Assigned Dosing Interval at Week 36 for Patients Eligible for Interval Extension[c]



[a]FAS. LS means were generated using a mixed model for repeated measures with baseline BCVA as a covariate; treatment group (aflibercept 8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asian-Pacific vs Europe vs America], BL BCVA [<60 vs ≥60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between baseline BCVA and visit and treatment and visit. [b]Observed values (censoring data post-ICE). [c]Safety analysis set, patients who completed Week 36.